Interview

Applicants are grateful for the personal interview granted to the undersigned and Robert Barker of Sepracor on December 12, 2006, the substance of which has been recorded in the interview summary prepared by the Examiner.

Claim Rejections – 35 U.S.C. § 112

The Examiner has maintained the rejection of Claims 2-5 and 12-14 as allegedly failing to comply with the enablement requirement of 35 U.S.C. § 112, first paragraph. Applicants respectfully maintain that these claims are enabled by the specification.

The subject matter of Claims 2-5 and 12-14 relates to the compound levalbuterol L-tartrate when it is in crystalline form, not to the crystalline form(s) of levalbuterol L-tartrate. The compound needs to be in crystalline form in order to be used in an aerosol formulation adapted for administration using a metered dose inhaler (cf. Claims 7 to 11). The specification teaches how to make levalbuterol L-tartrate in crystalline form and how to use it in a metered dose inhaler.

It is well established in patent law that a claim to a compound properly reads on the compound in any form, including the compound in a form or composition that has yet to be invented. It is also established that a claim may recite that a compound be in a particular form. The Examiner's attention is drawn, for example, to claim 1 of US 6,475,467 (one of the references cited by the Examiner under 35 USC 103). Claim 1 of US 6,475,467 reads on a formulation comprising any of the possible polymorphs of each of the recited compounds, and indeed of "active compounds" that have yet to be invented.

It is therefore respectfully submitted that Claims 2-5 and 12-14 comply with the enablement requirement of 35 U.S.C. § 112, first paragraph.

Claim Rejections - 35 U.S.C. § 103

Claims 1-14 and 17 stand rejected under 35 U.S.C. § 103(a) as allegedly being unpatentable over US20040202616 in view of WO 00/07567 as evidenced by US 6,475,467.

It is respectfully submitted that a person skilled in the art would not have conceived of making the claimed compound, levalbuterol L-tartrate. Moreover, as will be described below, and supported by the enclosed declaration, levalbuterol L-tartrate has unexpectedly advantageous properties - properties that have enabled the commercialization of a metered dose inhaler for administering levalbuterol.

1. Levalbuterol L-tartate was not obvious, *prima facie*.

As described at page 2, lines 25 to 27, of the present specification, the claimed compound contains half a mole of L-tartaric acid per mole of levalbuterol. Although L-tartaric acid is known, amongst many others, as a pharmaceutically acceptable acid, there is nothing in the cited references that would have motivated a person skilled in the art to prepare this particular salt. The hydrochloride salt was already known. It is commercially available (see page 1, lines 11 to 17 of the present specification). Another salt, the sulfate, is named in US 2004/0202616 in paragraph 0030 on page 4 and in US 6,475,467 at column 4, line 55 of US 6,475,467, but is not exemplified in either reference. Possibly the inventors of those cases never obtained and tested the sulfate salt, but named it as an example of a salt

of levalbuterol, because they knew that the racemate, albuterol, is commercially available as the sulfate. However, levalbuterol sulfate in crystalline form should not have been expected to have the same properties as albuterol sulfate in crystalline form. What is clear is that it was only the sulfate salt that they chose to name as an example of a salt of levalbuterol to use in their invention, not any tartrate salt, and certainly not any L-tartrate salt.

It is therefore respectfully submitted that a person skilled in the art would not have been motivated to make levalbuterol L-tartarte. The evidence of the references cited by the Examiner supports the view that others thinking of administering levalbuterol using a metered dose inhaler conceived of using the sulfate salt.

2. Levalbuterol L-tartate possesses unexpected properties.

Prior to the present invention, it was known to deliver levalbuterol into the lungs of patients as a solution of the hydrochloride salt using a nebuliser.

The Applicants sought a way to deliver levalbuterol into the lungs of patients using a metered dose inhaler.

In order to be able to deliver an active ingredient into the lungs of patients using a metered dose inhaler, it is necessary to provide particles that meet some very demanding criteria. These criteria are described in the paragraph bridging pages 1 and 2 of the present specification. The hydrochloride salt affords a crystalline solid, but unfortunately crystal particles of this salt were found not to meet the criteria. Furthermore, crystal particles of the sulfate salt, the salt named in the references cited by the Examiner, were also found to be unsuitable.

The present invention provides a salt of levalbuterol that affords crystalline particles suitable for administration using a metered dose inhaler. The suitability of the particles is evidenced by the fact that the invention has been commercialized. The commercial metered dose inhaler product was demonstrated to the Examiner during the interview on December 12, 2006.

Given that neither the hydrochloride salt nor the sulfate salt had been found to afford suitable crystalline particles, and that there was no reason to suppose that the deficiencies in these salts would be remedied by making the L-tartrate salt, it is respectfully submitted that the present invention was unexpected and therefore non-obvious.

Applicants submit herewith a Declaration under Rule 132 by Dr Paul McGlynn, one of the inventors named in this application, which describes experiments measuring the properties of the hydrochloride, sulfate and L-tartrate salts. The Examiner will note from this declaration that the sulfate salt was initially developed for commercialization, but the development was discontinued after the crystals were found to aggregate on storage. The crystals of the L-tartrate salt are not only stable in the presence of the components of the aerosol formulation, but most unusually have an aerodynamically-desirable needle shape that is retained when the crystals are micronized.

In addition, as described in the application at page 6, lines 15 to 27, and in the FDA-approved label for the product, which may be inspected on Sepracor Inc's website, levalbuterol L-tartrate has also been found to give lower systemic exposure to (R)-albuterol compared with albuterol sulfate.

It is therefore respectfully submitted that the presently claimed invention would not have been obvious to a person skilled in the art.

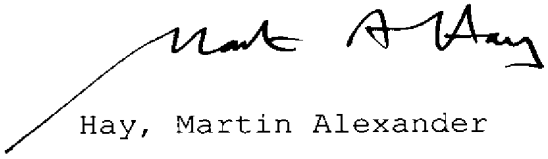
Conclusion

Applicants respectfully submit that the present application is in order to receive a Notice of Allowance.

Communication by Telephone

The undersigned's office is located in the United Kingdom, and hence the Examiner may have difficulty contacting him from the USPTO by telephone. If the Examiner wishes to speak with the undersigned by telephone, the undersigned can be contacted by e-mail at martinahay@martin-a-hay.com and will call the Examiner as soon as possible. Alternatively, he can make contact by calling Robert Barker at Sepracor on 508 357 7304.

Respectfully submitted,



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